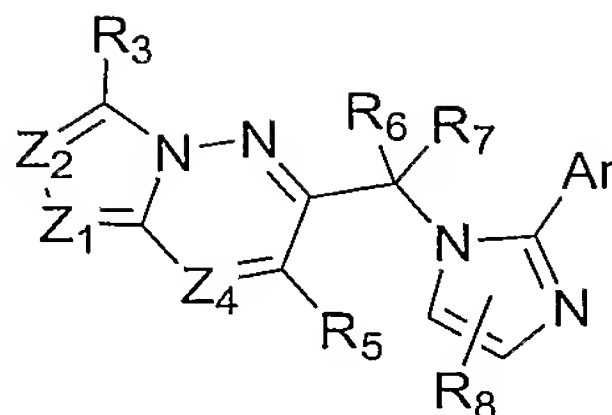


What is claimed is:

1. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

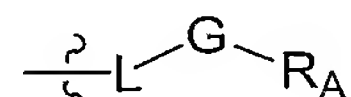
Z₁ is nitrogen or CR₁ and Z₂ is nitrogen or CR₂; such that at least one of Z₁ and Z₂ is nitrogen;

Z₄ is nitrogen or CR₄;

R₁, R₂, R₃ and R₄ are each independently selected from:

(a) hydrogen, halogen, nitro and cyano; and

(b) groups of the formula:



wherein:

L is a single covalent bond or C₁-C₈alkylene;

G is a single covalent bond, N(R_B), O, C(=O), C(=O)O, C(=O)N(R_B), N(R_B)C(=O), S(O)_m, CH₂C(=O), S(O)_mN(R_B) or N(R_B)S(O)_m; wherein m is 0, 1 or 2; and

R_A and each R_B are independently selected from:

(i) hydrogen; and

(ii) C₁-C₈alkyl, C₂-C₈alkenyl, C₂-C₈alkynyl, (C₃-C₈cycloalkyl)C₀-C₄alkyl, (3- to 6-membered heterocycloalkyl)C₀-C₄alkyl, (aryl)C₀-C₂alkyl and (heteroaryl)C₀-C₂alkyl, each of which is substituted with from 0 to 4 substituents independently selected from halogen, hydroxy, nitro, cyano, amino, C₁-C₄alkyl, C₁-C₄alkoxy, C₁-C₄alkanoyl, mono- and di(C₁-C₄alkyl)amino, C₁-C₄haloalkyl and C₁-C₄haloalkoxy;

R₅ is hydrogen, halogen, cyano, C₁-C₆alkyl, C₂-C₆alkenyl, C₂-C₆alkynyl, C₁-C₄alkoxy, or mono- or di-(C₁-C₄alkyl)amino, each of which is substituted with from 0 to 5 substituents independently chosen from halogen, hydroxy, nitro, cyano, amino, C₁-C₄alkoxy, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, mono- and di-C₁-C₄alkylamino, C₃-C₈cycloalkyl, phenyl, phenylC₁-C₄alkoxy and 5- or 6-membered heteroaryl;

R₆ and R₇ are independently hydrogen, methyl, ethyl or halogen;

R₈ represents 0, 1 or 2 substituents independently chosen from halogen, hydroxy, nitro, cyano, amino, C₁-C₄alkyl, C₁-C₄alkoxy, mono- and di(C₁-C₄alkyl)amino, C₃-C₇cycloalkyl, C₁-C₂haloalkyl and C₁-C₂haloalkoxy; and

Ar represents phenyl, naphthyl or a 5- to 10-membered heteroaryl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, hydroxy, nitro, cyano, amino, C₁-C₈alkyl, C₁-C₈alkenyl, C₁-C₈alkynyl, C₁-C₈alkoxy, (C₃-C₇cycloalkyl)C₀-C₄alkyl, (C₃-C₇cycloalkyl)C₁-C₄alkoxy, C₂-C₈alkyl ether, C₃-C₈alkanone, C₁-C₈alkanoyl, 3- to 7-membered heterocycloalkyl, C₁-C₈haloalkyl, C₁-C₈haloalkoxy, oxo, C₁-C₈hydroxyalkyl, C₁-C₈aminoalkyl, and mono- and di-(C₁-C₈alkyl)aminoC₀-C₈alkyl.

2. A compound or salt according to claim 1, wherein R₈ represents 0 or 1 substituent selected from halogen, C₁-C₂alkyl and C₁-C₂alkoxy.

3. A compound or salt according to claim 1 or claim 2, wherein Ar is substituted with 0, 1, 2 or 3 substituents independently selected from halogen, hydroxy, amino, cyano, C₁-C₄alkyl, C₁-C₄alkoxy, mono- or di-C₁-C₄alkylamino, C₂-C₄alkanoyl, (C₃-C₇cycloalkyl)C₀-C₂alkyl, C₁-C₂haloalkyl and C₁-C₂haloalkoxy.

4. A compound or salt according to claim 1 or claim 2, wherein Ar represents phenyl, pyridyl, thiazolyl, thienyl, pyridazinyl or pyrimidinyl, each of which is substituted with from 0 to 4 substituents.

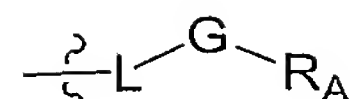
5. A compound or salt according to claim 4, wherein Ar represents phenyl, pyridyl, thiazolyl, thienyl or pyridazinyl, each of which is substituted with from 0 to 3 substituents independently selected from chloro, fluoro, hydroxy, cyano, amino, C₁-C₄alkyl, C₁-C₄alkoxy, C₁-C₂alkylamino, C₁-C₂haloalkyl and C₁-C₂haloalkoxy.

6. A compound or salt according to claim 5, wherein Ar represents phenyl, 2-pyridyl, 1,3-thiazol-2-yl, 2-thienyl or pyridazin-3-yl, each of which is substituted with from 0 to 3 substituents independently selected from fluoro, chloro, hydroxy, C₁-C₂alkyl, cyano and C₁-C₂alkoxy.

7. A compound or salt according to claim 5, wherein Ar represents 2,6-difluoro-phenyl, 2,5-difluoro-phenyl, 5-fluoro-2-methyl-phenyl, pyridine-2-yl, 3-fluoro-pyridin-2-yl, 3-cyano-pyridin-2-yl, 3-trifluoromethyl-pyridin-2-yl, 3-hydroxy-pyridin-2-yl, 3-methoxy-pyridin-2-yl, 6-fluoro-pyridin-2-yl, 6-cyano-pyridin-2-yl, 6-trifluoromethyl-pyridin-2-yl, 6-hydroxy-pyridin-2-yl or 6-methoxy-pyridin-2-yl.

8. A compound or salt according to any one of claims 1-7, wherein R₁, R₂, R₃ and R₄ are independently selected from:

- (a) hydrogen, halogen or cyano; and
- (b) groups of the formula:



wherein:

- (i) L is a single covalent bond;
- (ii) G is a single covalent bond, -NH-, -N(R_B)-, -O-, -C(=O)O- or C(=O)-; and
- (iii) R_A and R_B are independently selected from (1) hydrogen and (2) C₁-C₆alkyl, C₂-C₆alkenyl, (C₃-C₇cycloalkyl)C₀-C₂alkyl, phenyl, thienyl, pyridyl, pyrimidinyl, thiazolyl and pyrazinyl, each of which is substituted with from 0 to 4 substituents independently selected from hydroxy, halogen, cyano, amino, C₁-C₂alkyl and C₁-C₂alkoxy.

9. A compound or salt according to claim 8 wherein R₁, R₂, R₃ and R₄ are independently selected from hydrogen, hydroxy, halogen, cyano, aminocarbonyl, C₁-C₆alkyl, C₁-C₆alkoxy, C₂-C₆alkyl ether, C₃-C₇cycloalkyl, C₁-C₄hydroxyalkyl, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, C₁-C₆alkoxycarbonyl, mono- and di-(C₁-C₄alkyl)amino, phenyl and pyridyl.

10. A compound or salt according to claim 9, wherein R₃ and R₄ are independently selected from hydrogen, methyl and ethyl.

11. A compound or salt according to any one of claims 1-10, wherein Z_1 is nitrogen and Z_2 is CR_2 .

12. A compound or salt according to claim 11, wherein R₂ is selected from hydrogen, cyano, aminocarbonyl, C₁-C₄alkyl, C₁-C₄alkoxy, C₁-C₄alkoxycarbonyl, C₂-C₄alkyl ether, C₃-C₇cycloalkyl, C₁-C₂hydroxyalkyl, fluoromethyl, difluoromethyl, trifluoromethyl, phenyl and pyridyl.

13. A compound or salt according to any one of claims 1-10, wherein Z_1 is CR_1 and Z_2 is nitrogen.

14. A compound or salt according to claim 13, wherein R₁ is selected from hydrogen, cyano, aminocarbonyl, C₁-C₄alkyl, C₁-C₄alkoxy, C₁-C₄alkoxycarbonyl, C₂-C₄alkyl ether, C₃-C₇cycloalkyl, C₁-C₂hydroxyalkyl, fluoromethyl, difluoromethyl, trifluoromethyl, phenyl and pyridyl.

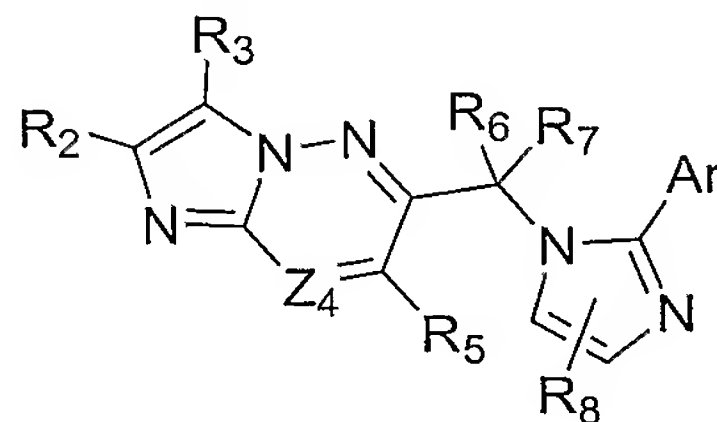
15. A compound or salt according to any one of claims 1-10, wherein Z_1 and Z_2 are nitrogen.

16. A compound or salt according to any one of claims 1-15, wherein R₆ and R₇ are both hydrogen.

17. A compound or salt according to any one of claims 1-16, wherein R_5 is C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_1 - C_4 alkoxy, or mono- or di- C_1 - C_4 alkylamino, each of which is substituted with from 0 to 2 substituents independently selected from halogen, hydroxy, C_1 - C_2 alkoxy, C_3 - C_8 cycloalkyl, phenyl and phenyl C_1 - C_2 alkoxy.

18. A compound or salt according to claim 17, wherein R_5 is ethyl, propyl, butyl, ethoxy or methoxymethyl.

19. A compound or salt according to claim 1, wherein the compound has the formula:



wherein:

R_2 is selected from hydrogen, hydroxy, halogen, cyano, aminocarbonyl, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, C_3 - C_7 cycloalkyl, C_2 - C_6 alkyl ether, C_1 - C_4 hydroxyalkyl, C_1 - C_2 haloalkyl, C_1 - C_2 haloalkoxy, C_1 - C_4 alkoxycarbonyl, mono- and di- $(C_1$ - C_4 alkyl)amino, phenyl and pyridyl;

R_3 and R_4 , if present, are independently hydrogen or C_1 - C_4 alkyl;

R_5 is C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_1 - C_4 alkoxy, or mono- or di- C_1 - C_4 alkylamino, each of which is substituted with from 0 to 2 substituents independently selected from halogen, hydroxy, C_1 - C_2 alkoxy, C_3 - C_8 cycloalkyl, phenyl and phenyl C_1 - C_2 alkoxy;

R_6 and R_7 are independently hydrogen, methyl, ethyl or halogen;

R_8 represents 0 or 1 substituent selected from halogen, C_1 - C_2 alkyl and C_1 - C_2 alkoxy; and

Ar represents phenyl, 2-pyridyl, 1,3-thiazol-2-yl, 2-thienyl or 3-pyridazinyl, each of which is substituted with from 0 to 3 substituents independently selected from fluoro, chloro, hydroxy, C_1 - C_2 alkyl, C_1 - C_2 haloalkyl, cyano and C_1 - C_2 alkoxy.

20. A compound or salt according to claim 19, wherein:

R_2 is hydrogen, cyano, aminocarbonyl, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, C_3 - C_6 cycloalkyl, C_2 - C_6 alkyl ether, C_1 - C_4 hydroxyalkyl, C_1 - C_2 haloalkyl or C_1 - C_4 alkoxycarbonyl;

Z_4 is CR_4 ;

R_3 and R_4 are independently hydrogen or C_1 - C_2 alkyl;

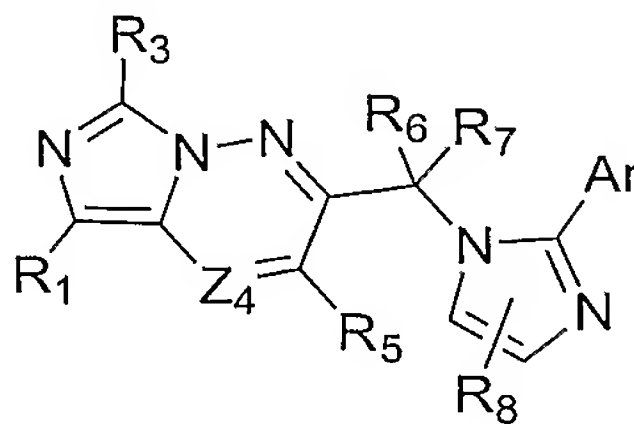
R_5 is C_1 - C_6 alkyl or C_2 - C_6 alkenyl, each of which is substituted with from 0 to 2 substituents independently selected from halogen, hydroxy and C_1 - C_2 alkoxy;

R_6 and R_7 are hydrogen;

R_8 represents 0 substituents; and

Ar represents phenyl or 2-pyridyl, each of which is substituted with from 0 to 3 substituents independently selected from fluoro, chloro, C₁-C₂alkyl, C₁-C₂haloalkyl, cyano and C₁-C₂alkoxy.

21. A compound or salt according to claim 1, wherein the compound has the formula:



wherein:

R₁ is selected from hydrogen, hydroxy, halogen, cyano, aminocarbonyl, C₁-C₆alkyl, C₁-C₆alkoxy, C₃-C₇cycloalkyl, C₂-C₆alkyl ether, C₁-C₄hydroxyalkyl, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, C₁-C₄alkoxycarbonyl, mono- and di-(C₁-C₄alkyl)amino, phenyl and pyridyl;

R₃ and R₄, if present, are independently hydrogen or C₁-C₄alkyl;

R₅ is C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₄ alkoxy, or mono- or di-C₁-C₄alkylamino, each of which is substituted with from 0 to 2 substituents independently selected from halogen, hydroxy, C₁-C₂alkoxy, C₃-C₈cycloalkyl, phenyl and phenylC₁-C₂alkoxy;

R₆ and R₇ are independently hydrogen, methyl, ethyl or halogen;

R₈ represents 0 or 1 substituent selected from halogen, C₁-C₂alkyl and C₁-C₂alkoxy; and

Ar represents phenyl, 2-pyridyl, 1,3-thiazol-2-yl, 2-thienyl or 3-pyridazinyl, each of which is substituted with from 0 to 3 substituents independently selected from fluoro, chloro, hydroxy, C₁-C₂alkyl, C₁-C₂haloalkyl, cyano and C₁-C₂alkoxy.

22. A compound or salt according to claim 21, wherein:

R₁ is hydrogen, cyano, aminocarbonyl, C₁-C₆alkyl, C₁-C₆alkoxy, C₃-C₆cycloalkyl, C₂-C₆alkyl ether, C₁-C₄hydroxyalkyl, C₁-C₂haloalkyl or C₁-C₄alkoxycarbonyl;

Z₄ is CR₄;

R₃ and R₄ are independently hydrogen or C₁-C₂alkyl;

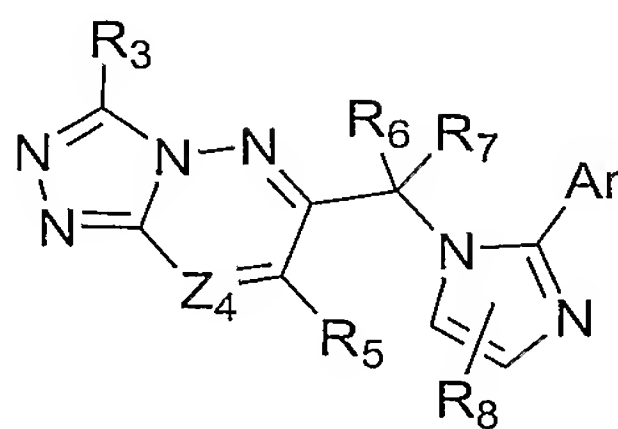
R₅ is C₁-C₆alkyl or C₂-C₆alkenyl, each of which is substituted with from 0 to 2 substituents independently selected from halogen, hydroxy and C₁-C₂alkoxy;

R₆ and R₇ are hydrogen;

R₈ represents 0 substituents; and

Ar represents phenyl or 2-pyridyl, each of which is substituted with from 0 to 3 substituents independently selected from fluoro, chloro, C₁-C₂alkyl, C₁-C₂haloalkyl, cyano and C₁-C₂alkoxy.

23. A compound or salt according to claim 1, wherein the compound has the formula:



wherein:

R₃ and R₄, if present, are independently hydrogen or C₁-C₄alkyl;

R₅ is C₁-C₆ alkyl, C₂-C₆ alkenyl, C₁-C₄ alkoxy, or mono- or di-C₁-C₄alkylamino, each of which is substituted with from 0 to 2 substituents independently selected from halogen, hydroxy, C₁-C₂alkoxy, C₃-C₈cycloalkyl, phenyl and phenylC₁-C₂alkoxy;

R₆ and R₇ are independently hydrogen, methyl, ethyl or halogen;

R₈ represents 0 or 1 substituent selected from halogen, C₁-C₂alkyl and C₁-C₂alkoxy; and

Ar represents phenyl, 2-pyridyl, 1,3-thiazol-2-yl, 2-thienyl or 3-pyridazinyl, each of which is substituted with from 0 to 3 substituents independently selected from fluoro, chloro, hydroxy, C₁-C₂alkyl, C₁-C₂haloalkyl, cyano and C₁-C₂alkoxy.

24. A compound or salt according to claim 23, wherein:

Z₄ is CR₄;

R₃ and R₄ are independently hydrogen or C₁-C₂alkyl;

R₅ is C₁-C₆alkyl or C₂-C₆alkenyl, each of which is substituted with from 0 to 2 substituents independently selected from halogen, hydroxy and C₁-C₂alkoxy;

R₆ and R₇ are hydrogen;

R₈ represents 0 substituents; and

Ar represents phenyl or 2-pyridyl, each of which is substituted with from 0 to 3 substituents independently selected from fluoro, chloro, C₁-C₂alkyl, C₁-C₂haloalkyl, cyano and C₁-C₂alkoxy.

25. A compound or salt according to any one of claims 1-24, wherein the compound exhibits a K_i of 1 micromolar or less in an assay of GABA_A receptor binding.

26. A compound or salt according to claim 25, wherein the compound exhibits a K_i of 100 nanomolar or less in an assay of GABA_A receptor binding.

27. A compound or salt according to claim 26, wherein the compound exhibits a K_i of 10 nanomolar or less in an assay of GABA_A receptor binding.

28. A pharmaceutical composition comprising a compound or salt according to any one of claims 1-24 in combination with a physiologically acceptable carrier or excipient.

29. A pharmaceutical composition according to claim 28, wherein the pharmaceutical composition is formulated as an injectible fluid, an aerosol, a cream, a gel, a pill, a capsule, a syrup or a transdermal patch.

30. A method for the treatment of anxiety, depression, a sleep disorder, attention deficit disorder or Alzheimer's dementia, comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or salt according to any one of claims 1-24.

31. A method for potentiating a therapeutic effect of a CNS agent, comprising administering to a patient a CNS agent and a compound or salt according to any one of claims 1-24.

32. A method for improving short term memory in a patient, comprising administering to a patient a therapeutically effective amount of a compound or salt according to any one of claims 1-24.

33. A method for altering the signal-transducing activity of GABA_A receptor, comprising contacting a cell expressing GABA_A receptor with a compound or salt according any one of claims 1-24 in an amount sufficient to detectably alter the electrophysiology of the cell, and thereby altering GABA_A receptor signal-transducing activity.

34. A method according to claim 33, wherein the cell recombinantly expresses a heterologous GABA_A receptor, and wherein the alteration of the electrophysiology of the cell is detected by intracellular recording or patch clamp recording.

35. A method for determining the presence or absence of GABA_A receptor in a sample, comprising the steps of:

- (a) contacting a sample with a compound or salt according claim 1, under conditions that permit binding of the compound to GABA_A receptor;
- (b) removing the compound or salt that is not bound to GABA_A receptor; and
- (c) detecting a level of the compound or salt bound to GABA_A receptor;

and therefrom determining the presence or absence of GABA_A receptor in the sample.

36. A method according to claim 35, wherein the presence or absence of bound compound is detected using autoradiography.

37. A method for determining the presence or absence of GABA_A receptor in a sample, comprising:
determining background binding by, in order:

- (a) contacting a first sample with a measured molar concentration of a labeled compound that is known not to bind to GABA_A receptors, under conditions that permit binding of compounds to GABA_A receptors;
 - (b) washing the first sample under conditions that permit removal of compounds that are not bound to GABA_A receptors; and
 - (c) detecting as a background binding amount an amount of label remaining after washing;
- and
- determining GABA_A binding by, in order:
- (d) contacting with a labeled compound or salt according to claim 1 a second sample matched to the first sample, said compound or salt being present at the measured molar concentration of (a) and said contacting being carried out under the conditions used in (a);
 - (e) washing the second sample under the conditions used in (b),
 - (f) detecting an amount of label remaining in the second sample after washing; and
 - (g) subtracting the background binding amount determined in (c) from the amount of label remaining in the second sample determined in (f)
- wherein the remainder of a positive amount after the subtraction of (g) indicates the presence of GABA_A receptor in the second sample.

38. A method according to claim 37, wherein the amount of label remaining after washing of the first sample and the second sample is detected using autoradiography.

39. A packaged pharmaceutical preparation comprising a pharmaceutical composition according to claim 28 in a container and instructions for using the composition to treat a patient suffering from anxiety, depression, a sleep disorder, attention deficit disorder, Alzheimer's dementia or short-term memory loss.

40. The use of a compound or salt according to claim 1 for the manufacture of a medicament for the treatment of a condition selected from anxiety, depression, a sleep disorder, an attention deficit disorder, Alzheimer's dementia and short-term memory loss.

41. 6-[2-(6-fluoro-pyridin-2-yl)-imidazol-1-ylmethyl]-7-propyl-imidazo[1,2-b]pyridazine or a pharmaceutically acceptable salt thereof.

42. 2-tert-butyl-6-[2-(6-fluoro-pyridin-2-yl)-imidazol-1-ylmethyl]-7-propyl-imidazo[1,2-b]pyridazine or a pharmaceutically acceptable salt thereof.

43. 2-ethyl-6-[2-(6-fluoro-pyridin-2-yl)-imidazol-1-ylmethyl]-7-propyl-imidazo[1,2-b]pyridazine or a pharmaceutically acceptable salt thereof.

44. 2-methyl-6-[2-(6-fluoro-pyridin-2-yl)-imidazol-1-ylmethyl]-7-propyl-imidazo[1,2-b]pyridazine or a pharmaceutically acceptable salt thereof.

45. 6-[2-(6-fluoro-pyridin-2-yl)-imidazol-1-ylmethyl]-7-propyl-2-trifluoromethyl-imidazo[1,2-b]pyridazine or a pharmaceutically acceptable salt thereof.

46. 6-[2-(6-fluoro-pyridin-2-yl)-imidazol-1-ylmethyl]-7-propyl-imidazo[1,2-b]pyridazine-2-carboxylic acid ethyl ester or a pharmaceutically acceptable salt thereof.

47. 6-[2-(6-fluoro-pyridin-2-yl)-imidazol-1-ylmethyl]-7-propyl-imidazo[1,2-b]pyridazine-2-carboxylic acid amide or a pharmaceutically acceptable salt thereof.

48. 6-[2-(6-fluoro-pyridin-2-yl)-imidazol-1-ylmethyl]-7-propyl-imidazo[1,2-b]pyridazine-2-carbonitrile or a pharmaceutically acceptable salt thereof.

49. 6-[2-(6-fluoro-pyridin-2-yl)-imidazol-1-ylmethyl]-8-methyl-7-propyl-imidazo[1,2-b]pyridazine or a pharmaceutically acceptable salt thereof.

50. 2-[2-(6-fluoro-pyridin-2-yl)-imidazol-1-ylmethyl]-5-methyl-3-propyl-imidazo[1,5-b]pyridazine or a pharmaceutically acceptable salt thereof.

51. 7-ethyl-6-[2-(3-fluoro-phenyl)-imidazol-1-ylmethyl]-[1,2,4]triazolo[4,3-b]pyridazine or a pharmaceutically acceptable salt thereof.

52. 7-ethyl-6-[2-(3-fluoro-phenyl)-imidazol-1-ylmethyl]-3-methyl-[1,2,4]triazolo [4,3-b]pyridazine or a pharmaceutically acceptable salt thereof.